REMARKS/ARGUMENTS

Claims 1, 7-9, 17-19, 29-35 and 38-39 are pending.

Claims 1, 7-9, 17-19, 29-30, 32-35 and 38-39 are currently amended.

Claims 41-45 are added.

Support for the amendment to Claim 1 is found at page 11, lines 10-25 of the original specification.

Support for Claim 18 is found at page 21, lines 15-19.

Support for Claim 19 is found at page 21, lines 15-19 and at page 17, lines 1-22.

Support for Claim 41 is found at page 11, line 28 – page 12, line 7.

Support for Claims 42-44 is found in the currently canceled Claims 36-37.

The rejection of Claims 1, 7-8, 17-19 and 29-40 under 35 U.S.C. §112, first paragraph is respectfully traversed.

Applicants respectfully direct the Examiner's attention to the decision by the Board of Patent Appeals and Interferences (BPAI) of In re Sorenson 3 USPQ2d 1462 (BPAI 1987). In Sorenson, the Board overturned a rejection made under 35 U.S.C. § 112, first paragraph where the Examiner rejected claims on the grounds that the claim expressions did not appear in the original disclosure. The holding of Sorenson is that the Applicants' disclosure must **"reasonably convey to the skilled artisan that Appellant had possession of the subject matter now claimed."** Id. at 1464 (emphasis added). In dicta the Board stated "we are mindful that Appellants' specification need not describe the claimed invention in *ipsis verbus* to comply with a written description requirement" Id. at 1463, and "the test is whether the originally filed specification disclosure *reasonably* conveys to a person having ordinary skill that Applicant had possession of the subject matter later claimed." Id. at 1464 citing to In re Kaslow 217 U.S.P.Q. 1089 (CAFC 1983).

Thus, the decision in Sorenson makes clear that the support for particular claim limitations is taken from the entirety of the specification.

As noted above, support for the amendments to Claim 1 finds **explicit, literal** support on page 11, lines 10-25. Specifically, page 11, lines 10-12 describes (emphases added):

> In preferred sulfonyl amino acid derivatives **according to formula I, Ar^1 is an unsubstituted or substituted phenyl**, preferably a 4-chlorophenyl group, X is preferably O, R^1, R^2, **R^3 and R^4 are preferably hydrogen**, n is 1, Ar^2 is preferably thienyl, R^5 is H or C_1-C_6-alkyl.

The Office maintains that the specification is limited to at least one of R^3 and R^4 to be an amino acid residue, and that defining both R^3 and R^4 to be hydrogen would constitute new matter. The Examiner has, however, acknowledged during the discussion held on May 4, 2004 that specific examples have both R^3 and R^4 specified as hydrogen (see Claim 9). Applicants also point out that at page 11, lines 11-12 of the specification, one embodiment of the invention is described wherein both R^3 and R^4 are hydrogen. Coupled with the **literal, explicit** support noted above AND the holding in Sorenson, *supra*, the definition of R^3 and R^4 as hydrogen in the present claims does not represent new matter and was described in the original specification in such a way as to reasonably convey to one of ordinary skill in the art that Applicants had possession of the claimed invention.

To the issue of the description of Ar^1 and "preferable 4-chlorophenyl group" in the specification on page 11, which was also raised in the Advisory Action, Applicants do not understand how the Examiner could have any confusion here. Specifically, page 11, lines 10-11 **clearly** describes that the Ar^1 is an unsubstituted or substituted phenyl (see this portion of the specification reproduced above). Set apart by commas, the Applicants also describe that one preferred embodiment of the Ar^1 group is a 4-chlorophenyl. This 4-chlorophenyl is a

narrower embodiment of a phenyl substituted with a halogen, in this case chloro, which again is unquestionably described on page 11, lines 10-12.

Additionally, the Office has maintained in the Advisory Action that newly added Claim 41 lacks antecedent basis. Applicants refer to the emphasized portion of page 11, lines 10-12 and page 13, line 24 – page 14, line 3 as shown previously. Clearly, the claimed compound is a preferred embodiment of the compound represented by Formula I, and the specification clearly states that "compounds pursuant to formula I" can indeed treat pathological states in which inhibition of JNK1 and/or JNK2 and/or JNK3 plays a critical role. Cancer and cardiovascular diseases are explicitly stated. Therefore, there is literal support for Claim 41. In addition, Applicants refer the Examiner's attention, again, to the Sorenson decision discussed above.

Applicants request withdrawal of the rejections.

The rejection of Claims 30-33 under 35 U.S.C. §101 is respectfully traversed.

The claims have been amended to clearly indicate the intended utility of the claimed method. Support for the amendment is found in the original specification (see page 1, lines 9-10). Additionally, in accordance with the Examiner's suggestions during the discussion with the Applicants' representatives on May 4, 2004, the phrase "modulating" has been replaced with "to down-regulate or inhibit," and is supported in the original specification (see page 5, line 8).

However, the Examiner suggests, in the Advisory Action, that changing "modulating" to "down-regulate or inhibit" introduces new matter and new issues and would be considered reach through claims and incredible utility. In addition, the Examiner alleges that Claims 42-45 are considered as "reach through claims and is incredible."

Claim 33 and the claims dependent from Claim 33 are directed to the treatment of a disorder of the autoimmune and/or neuronal system. Claims 42 and 43 are to a method of treating cancer. Claims 44 and 45 are directed to a method of treating cardiovascular disease.

Applicants respectfully direct the Examiner's attention to MPEP §2164.07(I)(B):

> The Examiner has the initial burden of challenging an asserted utility. Only after the Examiner has provided evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the Applicant to provide rebuttal evidence sufficient to convince one of ordinary skill in the art of the invention's asserted utility. *In re Brana* 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (citing *in re Bundy*, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981)

The specification clearly asserts the utility of the compound of formula (I) on page 13, line 24 – page 14, line 3 (emphasis added):

> Specifically, **the compounds pursuant to formula I are useful for the treatment or prevention of** immuno- and/or neuronal-related diseases or **pathological states** in which **inhibition of JNK1 and/or JNK2 and/or JNK3 plays a critical role** such as epilepsy; neurodegenerative diseases including Alzheimer's disease, Huntington's disease, Parkinson's disease; retinal diseases; spinal cord injury; head trauma, autoimmune diseases including multiple Sclerosis, inflammatory bowel disease (IBD), rheumatoid arthritis; asthma; septic shock; transplant rejection; **cancers including breast, colorectal, pancreatic** and **cardiovascular diseases including stroke, cerebral ischemia, arterosclerosis, myocordial infarction, myocordial reperfusion injury**.

Further, these statements of utility are supported by the *in vitro* data provided in the present specification. The activities of the sulfonyl amino acid compounds according to formula I were assessed using biological assays to assess JNK2 and/or 3 inhibition by these compounds. The assays are described on pages 31-32 and the data are presented in the Table on page 31 (reproduced below):

Example	*JNK3*	*JNK2*	*p38*	*ERK2*
1	1.2	2.7	>30	>30
6	0.64	1.3	>30	>30

The Applicants report that these data indicate a selective inhibition of the target, i.e., JNK 2 and 3. Specifically on page 32, lines 13-18, the Applicants state:

> The values indicated in respect of JNK2 and 3, p38 and ERK2 refer to the IC_{50} (μM), i.e. the amount necessary to **achieve 50% inhibition of said target (e.g. JNK2)**. AS# denotes an exemplary test compound as set out with its number in the above examples. From the above table it could be derived that said test compounds according to formula I do have a significant effect both on JNK2 and 3, but virtually no effect onto p38 and ERK2, thus delivering a **quite selective inhibitory effect**.

The specification also descries that compounds according to the invention decrease production of IL-2 in an IL-2 release assay, see pages 33-34. Specifically, on page 34, lines 26-27, the specification reports that: "The result of this assay shows that various test compounds **decrease the production of IL-2 of more than 30%@3uM."**

In a c-Jun reporter assay (described on pages 36-37), the specification also shows that the test compounds "**inhibit more than 20% of the activity of JNK@10uM.**" (page 37, lines 11-12)

The data presented in the specification also include *in vivo* data. Specifically, on page 37, an LPS induced endotoxin shock in mice assay is described. From these experiments, the Applicants state: "The test compounds displayed considerable capability to reduce inflammation related cytokines." (page 37, lines 24-25).

Still further, the Applicants also describe "the ability of the JNK inhibitors described in formula I to protect cell death during a stroke event" in Gerbils (page 37, lines 28-30). The

results of these analyses are presented on page 39, lines 4-5: "The test compounds displayed considerable capability to **protect from neuronal apoptosis** during induced global ischemia."

The Examiner has not provided any evidence of record to conclude that one of ordinary skill in the art would have any basis for doubting the asserted utility for the claimed compounds or their use in the claimed method presented herein and discussed above.

Applicants also direct the Examiner's attention to MPEP §2164.02 which states:

> If the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate.

As noted above, the Examiner has presented no evidence demonstrating that one skilled in the art would doubt that the compounds of the present invention would treat the disorders recited in the pending claims. In the event, the Examiner could challenge the asserted utility, such a challenge would be rebutted by the significant evidence presented in the specification which demonstrates that the claimed compounds inhibit JNK 2 and 3, decrease production of IL-2, reduce inflammatory cytokines, and protect from neuronal apoptosis. Furthermore, it is submitted that one of ordinary skill in the art would recognize the test data shown in the specification, and outlined above, to correlate with the disease conditions recited in the claims and as set forth in the specification on pages 13-14. Further, as stated in this portion of the specification, one of ordinary skill in the art recognizes that JNK "plays a critical role" in a number of pathological states and therefore by demonstrating that the compounds of formula I, as claimed, inhibit JNK supports the methods of using the compounds in treatment protocols as claimed herein.

Withdrawal of the rejections is respectfully requested.

The rejection of Claims 1, 7-9, 17-19 and 29-40 under 35 U.S.C. §112, second paragraph is respectfully traversed.

The claims have been amended by changing the phrase "sulfonyl amino acid derivative" to "compound" according to the Examiner's suggestions. Withdrawal of the rejection is respectfully requested.

The rejection of Claims 1-8, 17-24 and 26-28 under 35 U.S.C. §102(e) over Thompson (US 6,503,901) or under 35 U.S.C. §102(e)(f)(g) over EP'011 (EP 1,085,011) is respectfully traversed.

Neither Thompson nor EP'011 discloses the compound of formula (I) as claimed in Claim 1. Withdrawal of the rejection is requested.

Applicants submit that the application is now in condition for allowance. Early notification of such allowance is earnestly solicited.

Respectfully submitted,

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